<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
<th>Location/Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>P113</td>
<td>High seroprevalence of human herpes virus 8 (HHV-8) antibodies among vertically HIV-infected pediatric patients living in Germany</td>
<td>Feiterna-Sperling, C; Königs, C; Notheis, G; Buchholz, B; Welzsaeccker, K; Eberle, J; Hofmann, J (Berlin, Germany)</td>
<td></td>
</tr>
<tr>
<td>P115</td>
<td>Hospital admissions of HIV-infected patients at a Lisbon reference centre: comparison among previously known and in-ward HIV-diagnosed patients</td>
<td>Miranda, A; Fernandes, D; Peres, S; Biague, Q; Salvador, R; Faria, M; Mansinho, K (Lisbon, Portugal)</td>
<td></td>
</tr>
<tr>
<td>P117</td>
<td>Reasons of hospitalization for HIV-positive patients in the Infectology Center of Latvia in the period from 2009 to 2011</td>
<td>Sture, G; Rozentale, B; Zeltina, I; Januskevica, I; Sangierzeja, A (Riga, Latvia)</td>
<td></td>
</tr>
<tr>
<td>P118</td>
<td>Dynamics of Epstein-Barr Virus DNA concentrations in whole blood of HIV-1-infected patients during primary HIV-1 infection</td>
<td>Steingrover, R; Bekker, V; Beld, M; Lange, J; Wolthers, K; Kuipers, T; Prins, J (Amsterdam, The Netherlands)</td>
<td></td>
</tr>
<tr>
<td>P119</td>
<td>Changing spectrum of clinical presentation in visceral leishmania in HIV+ patients: preliminary results from a clinical registry in Northern Italy</td>
<td>Cenderello, G; Pasa, A; Dusi, A; Dentone, C; Izzo, M; Toscanini, F; Del Bono, V; De Maria, A (Genoa, Italy)</td>
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**HIV-related Infections, Co-infections and Cancers: Tuberculosis**

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
<th>Location/Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>P120</td>
<td>Particularities of tuberculosis in HIV-infected patients: 10-year experience of a Portuguese hospital</td>
<td>Nunes, S; Coutinho, D; Maio, A; Velez, J; Freitas, F; Oliveira, C (Aveiro, Portugal)</td>
<td></td>
</tr>
<tr>
<td>P121</td>
<td>CYP2B6 G516T and ABCB-1 C3435T polymorphisms: implications for efavirenz-associated liver toxicity in HIV/tuberculosis co-infected Thai patients</td>
<td>Uttayamakul, S; Manosuthi, W; Likanonsakul, S; Shioda, T; Khumsmit, S (Nonthaburi, Thailand)</td>
<td></td>
</tr>
<tr>
<td>P122</td>
<td>Impact of pharmacogenetic markers of CYP2B6 and clinical factors on plasma efavirenz level in HIV/tuberculosis co-infected Thai patients</td>
<td>Manosuthi, W; Sukasem, C; Lueangnyomkul, A; Mankatitham, W; Thongyen, S; Nikamhang, S; Manosuthi, S; Sungkanuparph, S (Nonthaburi, Thailand)</td>
<td></td>
</tr>
<tr>
<td>P125</td>
<td>Characteristics of tuberculous meningitis in HIV-infected patients</td>
<td>Hristea, A; Mancluc, C; Zaharia-Kezdi, E; Dorobat, C; Arbune, M; Olaru, I; Jipa, R; Niculescu, I; Streinu-Cercel, A (Bucharest, Romania)</td>
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*Indicates presenting author.
High seroprevalence of human herpesvirus 8 (HHV-8) antibodies among HIV-infected pediatric patients living in Germany

C. Feiterna-Sperling1, C. Künsigs2, G. Notheis3, B. Buchholz4, K. Weiss:cker5, J. Eberle6, J. Hofmann7

1Department of Pediatric Pneumology and Immunology, 2Department of Obstetrics, 3Institute of Medical Virology, Charité – University Medicine, Berlin, Germany; 4Department of Pediatrics, Goethe University, Frankfurt, Germany; 5Dr. Von Haunersches Kinderhospital, 6Max von Pettenkofer-Institute, Ludwig-Maximilians University, Munich, Germany, 7Department of Pediatrics, Medical Faculty, Heidelberg University, Germany

Background

Human herpesvirus 8 (HHV-8) is the etiological agent for Kaposi Sarcoma (KS). HIV-infected adults with advanced immunodeficiency are at risk. HHV-8 infection is common in certain African countries and in the Mediterranean. Low seroprevalence rates of 3-4% were reported for healthy children living in United States and Germany1. Little is known about the prevalence of HHV-8 infection in HIV-infected children living in non-endemic areas.

Purpose of the study

To determine the prevalence of HHV-8 antibodies among HIV-1-infected pediatric patients in Germany and to evaluate their association with age, gender, ethnicity, and other demographic factors.

Methods

- Multi-center cross-sectional study conducted in four specialized care centers for HIV-infected children in Germany (Berlin, Frankfurt/Main, Mannheim, Munich)
- Inclusion of vertically HIV-infected children & adolescents who were regularly seen in one of the sites
- Stored frozen serum specimens were tested for lytic and latent HHV-8 antibodies using an immunofluorescence assay (IFA).
- Seropositivity was defined as a titer ≥1:16 for lytic and/or latent HHV-8 antibodies

In the study group, seroprevalence rates were significantly higher in children born in Africa, Asia or Eastern Europe (32/81 [39.5%]) compared to those born in Western Europe (19/133 [14.3%]) \( P < 0.01 \).

HHV-8 titers among the 51 patients who were seropositive for HHV-8 ranged from 1:16 to 1:1024. The distribution of HHV-8 antibody titers are shown in Figure 2.

Clinical symptoms of HHV-8 infection were reported to be uncommon; only one child had a history of KS at 2 years of age.

Conclusion

Vertically HIV-infected patients living in Germany showed a high seroprevalence of 23.8%. These rates were higher as expected in the normal pediatric population. Our findings suggest that HHV-8 infection occurred already in the first years of life indicating a future risk for HHV-8 associated malignancies. Further studies are in progress to determine HHV-8 seroprevalence data in different ethnic groups.

References:

HOSPITAL ADMISSIONS OF HIV INFECTED PATIENTS AT A LISBON REFERENCE CENTER: COMPARISON AMONG PREVIOUSLY KNOWN AND IN-WARD HIV DIAGNOSED PATIENTS

Miranda AC¹, Fernandes D¹, Biague Q², Salvado R³, Faria F³, Peres S¹, Mansinho K¹
¹ Centro Hospitalar de Lisboa Oriental, E.P.E. – Hospital de Egas Moniz – Serviço de Infectologia e Medicina Tropical;
² Hospital José Joaquim Fernandes – Serviço de Medicina; ³ HPP Hospital de Cascais Dr. José de Almeida – Serviço de Medicina

OBJECTIVES
Comparison of hospital admission causes for HIV-infected patients, at Infectious Diseases Service of a Central University Hospital in Lisbon, that occurred during a period of 3 consecutive years, from 1st January 2009 until 31st December 2011. Two main groups were considering:

Group A: patients with previously diagnosed HIV infection;

Group B: patients diagnosed with HIV infection during current in-ward stay.

RESULTS: During the study period, 1167 patients were admitted at the Infectious Diseases ward, of those 617 (52.9%) presented HIV infection (92% HIV-1 and 8% HIV-2).

DEMOGRAPHIC DATA:
Chart 1: Patient distribution / 2009-2011 (n=1167)

<table>
<thead>
<tr>
<th>Year</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>383</td>
<td>426</td>
<td>359</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group</th>
<th>Total</th>
<th>HIV positive</th>
<th>HIV negative</th>
<th>HIV infected</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>521</td>
<td>316</td>
<td>205</td>
<td>201</td>
</tr>
<tr>
<td>B</td>
<td>656</td>
<td>384</td>
<td>272</td>
<td>100</td>
</tr>
</tbody>
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EPIDEMIOLOGIC DATA:
Chart 5: HIV transmission route (n=617)

<table>
<thead>
<tr>
<th>Transmission Route</th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vertical</td>
<td>46.4%</td>
<td>39.0%</td>
</tr>
<tr>
<td>Heterosexual</td>
<td>17.2%</td>
<td>11.6%</td>
</tr>
<tr>
<td>Other</td>
<td>36.4%</td>
<td>49.4%</td>
</tr>
</tbody>
</table>

CLINICAL AND IMMUNOLOGIC DATA:
Chart 6: Immunologic status at admission (n=617)

<table>
<thead>
<tr>
<th>CD4 cell count</th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 50</td>
<td>54.9%</td>
<td>45.1%</td>
</tr>
<tr>
<td>50-200</td>
<td>30.5%</td>
<td>36.4%</td>
</tr>
<tr>
<td>201-350</td>
<td>10.3%</td>
<td>5.2%</td>
</tr>
<tr>
<td>351-500</td>
<td>4.2%</td>
<td>0.2%</td>
</tr>
<tr>
<td>&gt;500</td>
<td>0.5%</td>
<td>0.5%</td>
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</table>

<table>
<thead>
<tr>
<th>CD4 cell count</th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Late Presenters</td>
<td>24.0%</td>
<td>20.0%</td>
</tr>
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</table>

FINAL CONSIDERATIONS
This analysis evidenced that a significant percentage of HIV patients diagnosed at admission were late presenters. Slightly half of patients with previous known HIV infection were prescribed combined antiretroviral therapy (cART) and only a third presented with undetectable plasma HIV RNA.

Non-adherence to cART was a major concern in this population, found to be the most frequent reason to virologic failure. Respiratory tract infections had a significant clinical impact in both groups, justifying the importance of vaccination prevention strategies in immunocompromised individuals.
RESULTS

Within three years 1205 patients were hospitalized.
Patients distribution by HIV/AIDS stage

<table>
<thead>
<tr>
<th>Clinical categories/CD4</th>
<th>A</th>
<th>B</th>
<th>C</th>
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<tbody>
<tr>
<td>&gt;500c/mm³</td>
<td>79</td>
<td>22</td>
<td>41</td>
</tr>
<tr>
<td>499-200c/mm³</td>
<td>141</td>
<td>55</td>
<td>115</td>
</tr>
<tr>
<td>&lt;200c/mm³</td>
<td>75</td>
<td>119</td>
<td>558</td>
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In late AIDS stage 714 patients were hospitalized. For the treatment of these patients therapy ART, OI prophylactic treatment and OI therapy had to be included.

Most common cause of hospitalization was opportunistic diseases: tuberculosis, MAC, candidiosis, cryptococcosis, PCP:
- 2009.y. - 168 patients (47.8%)
- 2010.y. - 201 patients (51.4%)
- 2011.y. - 193 patients (41.9%)

Second most common cause of hospitalization was liver diseases—toxic hepatitis, liver cirrhosis:
- 2009.y. - 37 patients (10.5%)
- 2010.y. - 55 patients (14%)
- 2011.y. - 47 patients (10.1%)

Other reason of hospitalization were lower respiratory tract infections—bronchitis, pneumonias, what not be associated with opportunistic infections.

Only in 5.9% cause of hospitalization was acute retroviral syndrome.

In 4.4% hospitalization outcome was death, only in 0.2% cases of death was associated with non−AIDS diseases.

Average time of hospitalization was 12, 8 days.

CONCLUSIONS

1. Every year HIV positive patient hospitalisation count increases.
2. More often hospitalisation patients are in late stage of HIV infection and reason of hospitalisation is opportunistic infections,what extends time of hospitalisation and costs.
3. Recommended immunisation against VHB and St. Pneumoniae, which would protect against non−AIDS diseases.
4. Medical staff education needs to be updated, which would help to diagnose HIV infection in early stage of diseases.
Dynamics of Epstein-Barr Virus DNA Concentrations in Whole Blood of HIV-1-Infected Patients During Primary HIV-1 Infection

Radjin Steingrover1,2, Vincent Bekker1, Marcel Beld3, Joep Lange4, Katja Wolthers1, Taco Kuijpers1, Jan M. Prins1

1, Academical Medical Center; 2, VUMC Medical Center; 3, KIT Biomedical Research, Royal Tropical Institute; 4, Amsterdam Institute for Global Health; all in Amsterdam, The Netherlands

Background
In HIV-1 infected patients high Epstein-Barr virus (EBV) DNA concentrations in blood or plasma are present in an abnormally high frequency of up to 64% of patients tested. Two mechanisms have been suggested that explain the high EBV DNA loads in HIV patients. Stevens et al found serologic evidence that high EBV concentrations were due to impaired immunological control of latent as well as lytic EBV replication. In contrast, Pirio et al found that the increase in EBV DNA was present in 6/16 (38%) of untreated patients, 7/11 (64%) of patients who had interrupted cART at week 24 and 2/12 (17%) of patients who were still on cART (table 1). Patients that continued cART throughout week 48 had a significantly lower prevalence of EBV viremia (p < 0.05) and showed a trend towards a significantly lower mean EBV DNA concentration (p = 0.07). Individual EBV DNA loads are plotted in the figures separately for untreated patients (top), patients treated for 24 weeks (mid) and patients treated continuously (bottom).

Conclusions
Our study confirms the presence of elevated EBV DNA levels from the earliest phase of HIV-1 infection when immunity is still intact, and other mechanisms that are associated with increased EBV infection (cellular or compartmental immune control) are probably responsible for these changes. Early cART reduces EBV viremia at week 48 in patients initiating cART during PHI, although this small study needs confirmation.

The use of cART has greatly decreased the incidence of ANHL, but the frequent detection of high concentrations of EBV DNA may warrant continued monitoring for lymphoproliferative diseases and special attention for the role of EBV in their etiology. Given the variable presence of EBV DNA within subjects, a longer period of observation and more extensive investigations on markers of EBV replication may establish patterns of EBV viremia and assess the risk of developing EBV-related pathologies.

References
7. Grijsen ML, Steingrover R, Wolthers1, Taco Kuijpers1, Jan M. Prins1
9. Greten SG, Steingrover R, Wolthers1, Taco Kuijpers1, Jan M. Prins1

Results
39 patients entered the study of whom 16 remained untreated and 23 started cART. 11 of the 23 treated patients interrupted cART after 24 weeks of therapy, 12 remained on cART through week 48. CD4+ T-cell compartment or immunity are probably responsible for these changes. Early cART reduces EBV viremia at week 48 in patients initiating cART during PHI, although this small study needs confirmation.

Conclusion
The use of cART has greatly decreased the incidence of ANHL, but the frequent detection of high concentrations of EBV DNA may warrant continued monitoring for lymphoproliferative diseases and special attention for the role of EBV in their etiology. Given the variable presence of EBV DNA within subjects, a longer period of observation and more extensive investigations on markers of EBV replication may establish patterns of EBV viremia and assess the risk of developing EBV-related pathologies.
Background

Interactions between VL and HIV are defined since the beginning of AIDS era but the impact of HAART has completely changed the clinical pattern. To address these issues, a Regional Disease Register was established encompassing all Infectious Disease Units in a coastal area in Northern Italy. The Register has the primary aim of monitoring prospectively the diagnostic, clinical and therapeutic approach to VL in the region, and to identify possible critical areas where changes in perception and management might be required.

Immunosuppressed patients, HIV in a special way, represented a significant proportion of incident cases, with differences in clinical presentation and high incidence of recorded secondary episodes.

Aim of the present analysis was to evaluate and report on clinical presentation, diagnostic tools and treatment in HIV patients identified during the first 4 years of activity.

Results

A total of 65 episodes in 55 pts. (36 adult, 19 children) were accumulated: median age was 37.5 months in pediatric patients and 48.7 (38 in HIV+) years in adults. All children were immunocompetent, whereas adults included both immunocompetent (ICC-17) and immunosuppressed (ISS-19) patients.

HIV was the leading cause of immunosuppression (10 pts 59%) all pts. belonged to CDC class C and they sustained 15 cases of infection (5 relapse); 4 pts. were not on HAART and 4 on a failing regimen with persistent viremia.

Average CD4+ cell count and HIV viral load at first diagnosis were respectively 135 /ul ±101 and 6,974 x10^4 cp/ml (0-2,8 x10^5). No significant CD4 cell number differences at first diagnosis were present among who would not recur compared to those for whom a VL recurrence was observed.

Clinical presentation was heterogeneous: Fever(F)+Hepato-splenomegaly 8, F+Lymphoadenopathy 2, F+pancytopenia=2, Trombocitopenya=2, other present.=1.

Detection of urinary antigen and serology (IFAT) were the most frequently used diagnostic tools (respectively in 14/15 and 11/15 pts.). However bone marrow detection of intracellular parasites was performed only in 4/15 cases. Liposomal amphotericin B was the most frequently (98.2% of cases) prescribed drug with 100% clinical cure. VL relapses(n=5) represented a crucial finding with very singular issues: they occurred in 3 pts., and time to relapse presents a significant difference among ICC and ISS (Fig.1 panel A) but no difference exist among HIV+ and other causes of immunosuppression (Fig.1 panel B); CD4+ cell numbers at VL recurrence were not different compared to those for the pts. at baseline. Furthermore three deaths with VL were reported, all occurred in relapsing HIV+ pts. accounting for significant (15.8%) overall mortality among this group.

Conclusions

The main findings can be summarized as follows: clinical presentation among HIV pts. is heterogeneous with frequent recurrence. Moreover the use of both serology and urinary antigens for diagnostic consist in a reliable diagnostic procedure and could be very useful in patients not eligible for bone marrow aspiration.
Particularities of Tuberculosis in HIV Infected Patients
Ten Year Experience of a Portuguese Hospital

Nunes S., Maio A., Coutinho D., Velez J., Freitas F., Oliveira C.
Infectious Diseases Ward, Centro Hospitalar do Baixo Vouga - Aveiro - Portugal

Introduction: The incidence of tuberculosis (TB) has dramatically increased since the advent of the human immunodeficiency virus (HIV) pandemic. In Portugal, tuberculosis is still common in HIV negative patients, despite earlier diagnosis and countrywide directly observed therapy strategies.

Materials and Methods: With the purpose of comparing some demographic and clinical aspects of TB in HIV infected and uninfected patients, the authors reviewed the files of patients admitted with the diagnosis of tuberculosis between January/2002 and December/2011. Statistic analysis was performed with IBM® SPSS Statistics 20.

Results: During this time period, there were 234 cases of tuberculosis, 43 (18%) of which occurred in HIV infected patients.

The most common site of infection was the lung in both groups but extra-pulmonary TB was significantly more frequent in the HIV infected group (67% versus 59%, p < 0.01). There were 43 cases of TB in HIV infected patients. The mean CD4 count at TB diagnosis was 180 ± 177/mm³.

In 11 (25%) of the patients, HIV was diagnosed during the TB episode. In the majority of patients (60%), TB was the AIDS defining condition. In 26 (60%) of patients there was microbiologic confirmation of TB, namely by positive smear (69%), positive culture (46%) and molecular diagnostic techniques (27%).

While most patients were treated with a 4-drug standard regimen, 16 (37%) of cases received alternative treatment, either for drug interactions (21%) or drug resistance (16%) The mean duration of treatment was 8.5 ± 4.8 months and the majority of patients (58%) were considered cured. About one-third of patients was lost to follow-up (32%).

Tuberculosis is a heterogeneous disease, presenting accordingly to the host immune status. The risk of extrapulmonary and disseminated TB increases with HIV infection but, in this cohort, that didn’t seem to influence the length of hospitalization. When divided by the CD4 cell count at TB diagnosis, the group over 200 cells/mm³ shared the greater risk of extrapulmonary TB characteristic of the more severely immunosuppressed. The authors found that in a quarter of the patients HIV was diagnosed during the TB episode, thus supporting the need of HIV screening whenever TB occurs, allowing for earlier diagnosis and prompt start of antiretroviral therapy.

Background: Cytochrome P450 2B6 (CYP2B6) and ATP-binding cassette, sub-family B (ABC-B-1) play an important role in metabolism and transport of anti-retroviral therapy (ART) agents. CYP2B6 516TT and ABC-B-1 3435CT polymorphisms affected plasma efavirenz levels. Efavirenz based ART was proved to be beneficial in HIV/tuberculosis co-infection management; however, drug-drug interactions and toxicity are the major concerns. Factors affecting adverse drug events and liver toxicity were investigated in this study.

Methods: Seventy-one HIV patients with tuberculosis receiving efavirenz (600 mg/day) based ART were enrolled in the randomized trial: the N2R study in Bamrasnaradura Infectious Diseases Institute, Thailand. After 12 weeks of ART, 65 rifampicin recipients continued for the analysis of the factors influenced drug toxicity. Plasma efavirenz, serum levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) and total and direct bilirubins were determined. CYP2B6 and ABC-B-1 polymorphisms were genotyped by real-time PCR. Mann-Whitney U test was used to compare genotypes and laboratory parameters.

Results: CYP2B6 516TT and ABC-B-1 3435CT genotypes were found in 9 (13.85%) and 33 (50.77%) patients, respectively, while six (9.23%) carried both -516TT and 3435CT genotypes. Patients carrying 516TT genotype had significantly higher mean rank plasma efavirenz than GT and GG genotypes (54.78 vs. 29.50, p=1.97x10^-4) while those carrying 3435CT had slightly higher than CC and TT genotypes. Patients carrying both 516TT and 3435CT had higher mean rank efavirenz levels than those without these two genotypes (60.17 vs. 30.24, p=2.21x10^-4), with significantly different ALT as well as total and direct bilirubin levels (p=0.044, 0.009, 0.021, respectively).

Conclusion: CYP2B6 516TT and ABC-B-1 3435CT influenced plasma efavirenz levels and related to higher levels of ALT, total and direct bilirubin in patients with HIV/Tuberculosis which implication for drug toxicity. The results might be useful for personalized therapy due to their impact on ART adherence related to drug resistance and treatment failure.

Discussion & Conclusion

CYP2B6 516TT and ABC-B1 3435CT gene polymorphisms influenced the adverse drug effects. By comparing the plasma EFV and NVP concentrations and efficiencies between these 2 non-nucleoside reverse transcriptase inhibitor-based regimens in the randomized trial of HIV-infected patients receiving rifampicin, the EFV based ART proved to be beneficial in HIV/tuberculosis co-infection management (Manosuthi et al., 2009). When the plasma EFV and the serum levels of ALT, AST, ALP as well as total and direct bilirubins were determined at week 12 of ART, the ALT, total bilirubin and direct bilirubin were higher in patients carrying both 516TT and 3435CT genotypes than those without these polymorphisms. The drug-drug interactions and toxicity are the major concerns due to their effects on patient’s quality of life and the medication adherence. These problems can lead to drug resistance and treatment failure.

Materials and Methods

Seventy-one of ARV naïve HIV patients with active tuberculosis were enrolled in randomized control trial conducted at Bamrasnaradura Infectious Diseases Institute (BIDI). They received rifampicin containing anti-TB regimens and efavirenz (600 mg/day) based ART. After 12 weeks of ART, 65 rifampicin recipients continued for the analysis of the factors influenced drug toxicity. CYP2B6 and ABC-B-1 genotyping were done by real-time PCR and the plasma EFV concentrations were measured by high performance liquid chromatography (HPLC). Genomic DNA was extracted by using QIAamp® blood kit, (QIAGEN, Hilden, Germany). This study was approved by the institutional ethics committees of BIDI and the Ministry of Public Health, Nonthaburi, Thailand.

Results

CYP2B6 516TT and ABC-B-1 3435CT genotypes were found in 9 (13.85%) and 33 (50.77%) patients, respectively, while 6 (9.23%) carried both 516TT and 3435CT genotypes. Patients carrying 516TT genotype had significantly higher mean rank plasma efavirenz than GT and GG genotypes (54.78 vs. 29.50, p=1.97x10^-4) while those carrying 3435CT had slightly higher than CC and TT genotypes. Patients carrying both 516TT and 3435CT had higher mean rank efavirenz levels than those without these two genotypes (60.17 vs. 30.24, p=2.21x10^-4), with significantly different ALT, total and direct bilirubin levels (p=0.044, 0.009, 0.021, respectively).

Objective

To investigate whether CYP2B6 G516T and ABC-B1 C3435T affect the adverse drug events and liver toxicity in HIV/TB co-infected patients receiving rifampicin.
The comprehensive information of CYP2B6 polymorphisms, clinical factors, and drug-drug interaction on efavirenz concentration in HIV/tuberculosis (TB) co-infected patients is unknown.

Patients co-infected with HIV and tuberculosis were prospectively enrolled.

Inclusion criteria were: (1) HIV-infected individuals 18-60 years of age, (2) newly clinically diagnosed active tuberculosis, positive acid-fast staining or a positive culture for Mycobacterium tuberculosis, (3) treated with antituberculous regimen 4-12 weeks prior to enrollment, (4) naive to ART, (5) baseline CD4 cell count < 350 cells/mm³, and (6) participated and provided an informed consent.

A total of 139 HIV/TB adults, in which 101 received rifampicin-containing anti-TB regimen, were prospectively enrolled. The median (IQR) CD4 cell count was 42 (17-105) cells/mm³ and median (IQR) plasma HIV-1 RNA was 5.8 (5.4-6.3) log copies/mL.

At week 12, median (IQR) plasma efavirenz concentration of all 139 patients was 2.3 (1.4-3.9) mg/dL. The frequencies of heterozygous/homozygous mutant of SNPs were 64C>T (10%, 7%), 516G>T (35%), *1/*2 (7%), and *6/*6 (7%).

Haplotypes identified were *1/*6 (41%), *1/*1 (35%), *1/*4 (0.638, -0.864), *1/*2 (0.220, -1.262), 64C>T (0.105, -1.387), 516G>T <0.001, 2.149, 785A>G <0.001, 1.947, 1375A>G (0%, 0%), 1459C>T (3%, 0%), 3003C>T (44%, 27%), 18492T>C (39%, 6%), and 21563C>T (57%, 5%). The most three frequent CYP2B6 haplotypes identified were *1/*6 (41%), *1/*1 (35%), *1/*2 (7%), and *6/*6 (7%).

CONCLUSIONS
This study provides an interesting data regarding the potential factors contribute to pharmacokinetic variability of efavirenz in Thai patients co-infected with HIV and TB, those include genetic factor, biological factor (i.e., body weight), and environmental factor (i.e., efavirenz-rifampicin interactions). Difference of genetic polymorphism influences different CYP2B6 enzyme expression. The patients with particular haplotype and low body weight have the greatest probability of low plasma efavirenz concentration. Pharmacokinetic variability reflects the combined influence of such factors but in the different magnitudes.
Characteristics of tuberculous meningitis in HIV-infected patients

A. Hristea¹, C. Manciuc², IE. Zaharia-Kezdi³, C. Dorobat², M. Arbune⁴, ID Olaru¹, R. Jipa¹, I. Niculescu¹, A. Streinu-Cercel¹

1. Prof Dr Matei Bals National Institute for Infectious Diseases, Bucharest, RO; 2. Sf Parascheva Clinical Hospital for Infectious Diseases, Iasi, RO; 3. County Hospital Mures, Targu Mures RO; 4. Sf Paraschiva Clinical Hospital for Infectious Diseases, Galati, RO.

BACKGROUND

Tuberculosis meningitis (TBM) is a growing problem in HIV infected patients, especially in developing countries. Between 2007-2010, there were 476 reported cases of TBM in Romania, but with no data about their virological profile. There is still a large number of TBM cases (with severe prognosis) that implies an increased accountability measures in TB control in the territory.

Objective:

• Describe clinical and laboratory differences of tuberculous meningitis (TBM) in HIV-infected versus HIV non-infected patients
• Assess risk factors of death in HIV-infected patients.

METHODS

• Retrospective study of patients admitted with TBM between 2001-2011 in four infectious diseases hospitals. 
• Hospital records were reviewed and data on patient history, epidemiological characteristics, clinical findings including neurological examination, laboratory and imaging findings were analyzed.
• Patients were defined as having TBM according to a consensus definition published by Marais et al and further divided into three categories of TBM (definite, probable and possible).
• Patients were considered to have definite TBM if AFB were detected in the CSF, or they had a CSF culture or commercial nucleic acid amplification test (NAAT)positive for M. tuberculosis.
• Patients had probable TBM if they scored at least 10 points (and cerebral imaging was not available) or 12 points (when cerebral imaging was available).
• Possible TBM was diagnosed when a patient had a score of 6–9 points (cerebral imaging unavailable) or 6–11 points (cerebral imaging available).
• Differences between groups were analyzed using the Mann-Whitney U test for continuous variables and the chi-square test for dichotomous variables. Multivariable analysis was performed using binary logistic regression.

RESULTS

We identified 162 patients with TBM of which 47 (29%) tested positive for HIV infection. There was a male predominance in both groups. The overall male to female sex ratio was 1.8:1.

HIV infection was diagnosed before TBM episode in 35 (75%) patients. Twenty-four (51%) HIV-infected patients had concomitant extra – central nervous system tuberculosis (45% pulmonary TB) vs. forty-seven (41%) HIV non-infected patients (34% pulmonary TB).

TBM Categories HIV infected vs non-infected patients

Patient characteristics

AGE

- HIV infected: 22 (18-34)
- HIV non-infected: 34 (20-53)

- Duration of symptoms before admission (days): median (IQR)
  - HIV infected: 10 (7-14)
  - HIV non-infected: 10 (7-14)

- Cranial nerve palsy N (%)
  - HIV infected: 6 (13)
  - HIV non-infected: 31 (27)

- Meningeal syndrome N (%)
  - HIV infected: 34 (72)
  - HIV non-infected: 102 (89)

- Glasgow coma scale < 7 N (%)
  - HIV infected: 11 (23)
  - HIV non-infected: 18 (16)

- Cell number in CSF (cells/mm²) (median, IQR)
  - HIV infected: 180 (94-457)
  - HIV non-infected: 200 (86-600)

- Protein CSF level (mg/dl) (median, IQR)
  - HIV infected: 0 (130-542)
  - HIV non-infected: 178 (120-279)

- CSF/serum glucose < 0.5 N (%)
  - HIV infected: 32 (71)
  - HIV non-infected: 96 (84)

- In-hospital mortality N (%)
  - HIV infected: 18 (13)
  - HIV non-infected: 13 (11)

CD4 levels in HIV deceased vs survivor patients

- HIV infected: 28 (62%)
- HIV non-infected: 182 (50%)

In hospital mortality

- HIV infected: 25 (43%)
- HIV non-infected: 20 (18%)

CONCLUSIONS

Between the two groups there were no significant differences in terms of clinical (except meningeal syndrome) and laboratory findings. HIV infection does not alter the neurological features of tuberculous meningitis, but is associated with increased mortality in TBM patients. Although most of our patients with TBM were late presenters, death in HIV infected patients was associated with a lower median CD4 count.

REFERENCES